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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Application Number: 08/844,336

Filing Date: April 18, 1997

Appellant(s): CONTAG ET AL.

Dahna S. Pasternak
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed June 8, 2011 appealing from the Office action mailed April 5, 2011.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1, 5-6, 9, 21-22 and 25-27 are pending in the application.

Claims 1, 5-6, 9, 21-22 and 25-27 stand rejected.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN

REJECTIONS.” New grounds of rejection (if any) are provided under the subheading “NEW GROUNDS OF REJECTION.”

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant’s brief.

(8) Evidence Relied Upon

No evidence is relied upon by the examiner in the rejection of the claims under appeal.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-6, 9, 21-22 and 25-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons of record. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to a biodetector comprising: **a transmembrane fusion protein** comprising an extracellular ligand-specific moiety comprising an antibody and a membrane intracellular enzymatic signal-transforming domain which is a kinase; **a transducer**

protein; and a responsive element (transcription activation element) coupled to a reporter gene (e.g. luciferase) via said responsive element. Said biodetector may further comprise a bacterial cell.

The specification discloses a biodetector comprising a fusion protein consisting of an antibody heavy chain and an active domain of PhoQ, PhoP (signal transducer) and the *lux* operon coupled to the Pho promoter. This biodetector meets the written description provision of 35 USC 112, *first* paragraph. However, the aforementioned claims are directed to encompass biodetectors comprising limitless combinations of transmembrane fusion proteins (comprising an extracellular antibody domain and an intracellular enzymatic signal domain – i.e. kinases), transducers and reporter genes/operons. None of these biodetectors meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim. The transmembrane fusion protein of the claimed biodetector must be able to activate a given transducer via its intracellular enzymatic signal transforming domain upon the binding of the “ligand” to the extracellular antibody. The transducers must be able to trigger either directly or indirectly, the activation of a transcription activating element (promoter) to effect the activation of the responsive element (reporter gene or operon). The specification discloses that said transducer may be any molecule that can recognize and respond to a change in conformation, electrical charge, addition or subtraction of any chemical subgroup and is capable of triggering a detectable response (see page 16 of the specification). With the exception of the antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled to the *lux* operon as its responsive element, the specification is silent with regard to what specific combinations of transmembrane proteins, transducers and responsive elements would result in a functional biodetector.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of the aforementioned antibody/PhoQ based biodetector, the skilled artisan cannot envision the detailed chemical structure of the encompassed biodetectors, regardless of the complexity or simplicity of the method of screening for active components (isolation). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGFs were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that "...To fulfill the written description requirement, a patent specification must describe an invention and does so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

While the individual components of the instant invention may have been known in the art, the compatibility of said components which would give rise to a functional biodetector was not. The instant claims encompass biodetectors comprising limitless combinations of transmembrane

fusion proteins (comprising an extracellular ligand binding domain [i.e. antibody] and a membrane intracellular enzymatic signal domain [i.e. kinase]; transducers; and a responsive element (which generates a detectable light signal). The claimed biodetectors are composed of components that can be either prokaryotic or eukaryotic in nature. Consequently, the instant claims encompass the mixing and matching of thousands of different prokaryotic and eukaryotic elements that must work together to form a functional biodetector. The single functional embodiment (the antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled to the *lux* operon as its responsive element) utilizes bacterial elements and promoters in a bacterial biosensor. The instant claims, on the other hand, encompass the mixing and matching of prokaryotic and eukaryotic elements of in a fashion unique to the art. Said art is silent with regard to efficacy of using eukaryotic elements within a bacterial biosensor or vice versa. Moreover, a survey of the relevant art demonstrates an inability to introduce a complete eukaryotic signal transduction system in any bacterial cell which allows for functionality. The specification is silent to what specific combinations elements will work. On the contrary, the specification discloses that one has to screen for operative and inoperative embodiments at each level and provides no guidance as to what specific kinase would be functional in a given biodetector (see pages 26-28 of the specification). Consequently, the specification does not disclose any correlation between structure (i.e. the components of the biodetector) and function (the ability to function as a biodetector) as required by the written description requirement. Given the lack of guidance within the specification, the skilled artisan would not know what **combination of elements** would produce a biodetector that functions as claimed. Adequate written description requires more than a mere statement that it is part of the invention and *reference to a potential method for isolating it*. The functional fusion protein itself is required (see Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016).

Moreover, the biotechnology art as it relates to biodetectors not considered a “mature technology”. The crux of the *Capon* decision is what is known in the art. In the *Capon* decision, the CAFC stated “In summary, the Board erred in ruling that §112 imposes a *per se* rule requiring recitation in the specification of the nucleotide of claimed DNA when that sequence is already known in the field. However, the Board did not explore the support for each of the claims of both parties in view of the specific examples and general teachings in the specifications and the known science with application of precedent guiding review of the scope of the claims.” The CAFC determined that the correlation between structure and function, required to meet the written description requirements, were known in the art. This is not the case with regard to the instant claims as the specifics components of the claimed biodetector that would give rise to a functional biodetector are not known in the art. Consequently, the *Capon* decision is not germane to the instant rejection.

The claimed biodetectors are unrelated by structure, the genus of components making up said biodetectors is vast; there is no description of any core structure that meets the limitations of the instant claims. Mere function does not describe a structure, because the specification does not provide relevant identifying characteristics, including functional characteristics when coupled with known or disclosed correlation between function and structure. The courts have held that in these instances, the specification lacks written description see *Enzo Biochem Inc. v. Gen-Probe Inc.* 63 USPQ2D 1609 (CAFC 2002) and *University of Rochester v. G.D. Searle & Co.* 69 USPQ2D 1886 (CAFC 2004). When the genus is vast and compounds are claimed by function alone and the specification lacks a known or disclosed correlation between structure and

function, the written description of the specification does not convey possession of the claimed genus.

Additionally, possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. See *University of Rochester*, 358 F.3d at 927, 69 USPQ2d at 1895.

Therefore, only aforementioned antibody/PhoQ based biodetector, but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed is not representative of the genus because the genus is highly variant. Appellant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.).

(10) Response to Argument

Appellant argues:

1. The Examiner errs in construing the claimed subject matter as the claims specify that the claimed biodetectors must include an antibody-kinase fusion molecule.
2. Possession is demonstrated by detailed description of the components and the versatility provided by the selection of the extracellular antibody component.
3. The state of the art, as summarized in the specification, clearly evidences that the claimed antibody-kinase fusion proteins and their role in signal transduction were known.
4. Appellant strongly traverses the assertion that *Fiers v. Revel and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd* are not germane to the case on appeal.
5. The pending claims are directed to biodetectors that are literally described in the specification and whose components were described in the specification and known in the art.

6. In light of the holdings of the Federal Circuit, the Office's assertion that Appellants are required to disclose multiple examples of particular biodetectors is inconsistent with the requirements of the first paragraph of Section 112.
7. The Examiner has improperly based a written description rejection on the grounds that embodiments must be "empirically determined".
8. The biodetectors of dependent claims 5-6, 9, 21-22 and 25-27 are properly described.

Examiner Rebutts

With regard to Points 1-3, as set forth in the rejection, the claimed biodetector comprises 3 distinct elements: **a transmembrane fusion protein** comprising an extracellular ligand-specific moiety comprising an antibody and a membrane intracellular enzymatic signal-transforming domain which is a kinase; **a transducer protein**; and **a responsive element** (transcription activation element) coupled to a reporter gene (e.g. luciferase) via said responsive element. Not just an antibody-kinase fusion. The genus of components making up said biodetectors is vast and there is no description of any core structure that meets the limitations of the instant claims. Appellant is reminded that mere function does not describe a structure, because the specification does not provide relevant identifying characteristics, including functional characteristics when coupled with known or disclosed correlation between function and structure. The courts have held that in these instances, the specification lacks written description see *Enzo Biochem Inc. v. Gen-Probe Inc.* 63 USPQ2D 1609 (CAFC 2002) and *University of Rochester v. G.D. Searle & Co.* 69 USPQ2D 1886 (CAFC 2004). Additionally, when the genus is vast and compounds are claimed by function alone and the specification lacks

a known or disclosed correlation between structure and function, the written description of the specification does not convey possession of the claimed genus.

With regard to Point 2, the description of a single portion of a multicomponent entity is insufficient to properly describe said entity.

With regard to Point 3, contrary to Appellant's assertion, the cited portions of the specification the level of knowledge in the art with regard to antibody-kinase fusion proteins as said portions of the specification discuss only antibody-phosphatase fusion proteins which are not encompassed by the instant claims. Moreover, the single functional embodiment (the antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled to the *lux* operon as its responsive element) utilizes bacterial elements and promoters in a bacterial biosensor. The instant claims, on the other hand, encompass the mixing and matching of prokaryotic and eukaryotic elements of in a fashion unique to the art. Said art is silent with regard to efficacy of using eukaryotic elements within a bacterial biosensor or vice versa. Moreover, a survey of the relevant art demonstrates an inability to introduce a complete eukaryotic signal transduction system in any bacterial cell which allows for functionality. The specification is silent to what specific combinations elements will work.

With regard to Point 4, Appellant is incorrectly characterizing the Examiner's position. As clearly, set forth in the rejection, the Examiner accurately sets forth that adequate written description requires more than a mere statement that it is part of the invention and *reference to a potential method for isolating it*. The functional fusion protein itself is required (see Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016).

With regard to Point 5, the only biodetector "literally described" in the specification is the biodetector comprising a fusion protein consisting of an antibody heavy chain and an active domain

of PhoQ, PhoP (signal transducer) and the *lux* operon coupled to the Pho promoter. Moreover, while the individual components of the instant invention may have been known in the art, the compatibility of said components which would give rise to a functional biodetector was not. The instant claims encompass biodetectors comprising limitless combinations of transmembrane fusion proteins (comprising an extracellular ligand binding domain [i.e. antibody] and a membrane intracellular enzymatic signal domain [i.e. kinase], transducers and a responsive element which generates a detectable light signal). The claimed biodetectors are composed of components that can be either prokaryotic or eukaryotic in nature. Consequently, the instant claims encompass the mixing and matching of thousands of different prokaryotic and eukaryotic elements that must work together to form a functional biodetector. The single functional embodiment (the antibody/PhoQ based biodetector which utilizes PhoP as its transducer and the Pho promoter coupled to the *lux* operon as its responsive element) utilizes bacterial elements and promoters in a bacterial biosensor. The instant claims, on the other hand, encompass the mixing and matching of prokaryotic and eukaryotic elements of in a fashion unique to the art. Finally, the position that there is a total lack of correlation between structure and function is supported by the specification which clearly sets forth that one **has to screen for operative and inoperative embodiments at each level** (see pages 26-28 of the specification).

With regard to Point 6, the decisions cited by Appellant are based on what was known in the art. As set forth in the rejection, the instant claims encompass the mixing and matching of prokaryotic and eukaryotic elements of in a fashion unique to the art. Said art is silent with regard to efficacy of using eukaryotic elements within a bacterial biosensor or vice versa. Moreover, a survey of the relevant art demonstrates an inability to introduce a complete eukaryotic signal transduction system in any bacterial cell which allows for functionality. Appellant's position that one merely needs to know the components of

an entity to properly describe it is analogous to saying that all proteins meet the written description requirements because all of the component amino acids are known in the art. This position, contrary to Appellant's assertion, is not supported by either case law or the statutes.

With regard to Point 7, the rejection, contrary to Appellant's assertion, is based on a lack of correlation between structure and function as required by the written description requirement. Neither the specification nor the art provides said correlation. This fact is acknowledged by the instant specification which states clearly sets forth that one has to screen for operative and inoperative embodiments at each level (see pages 26-28 of the specification).

With regard to Point 8, none of the rejected dependent claims are drawn to embodiments that convey a correlation between structure and function. Said claims merely recite differing portions of the claimed biodetector but never all the components.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/ROBERT A ZEMAN/

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